SnapShot: NR Coregulators

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Coregulator/ Family*	Symbols	Interactions (Nuclear Receptors)	Functions	Disease Links	Interactions (Coregulators)	Interactions (Others)
Steroid receptor coactivators*	SRC-1/NCOA1; SRC-2/NCOA2; (GRIP1, TIF2); SRC-3/NCOA3; (AIB1, ACTR, TRAM-1, RAC3)	**SRC-1** AR, COUP-TFI, CAR, ERα, ERβ, ERRγ, FXRα, GR, HNF4α, PPARα, PPARγ, PXR, PR, RORβ, RARα, RARβ, RXRα, RXRβ, SF-1, TRα, TRβ, EAR	Coactivators for the NR superfamily and other transcription factors; roles in reproductive development and metabolism. **Domains:** PAS/ bHLH, acetyltransferase	Up-regulated in cancer	**SRC-1** ASC-1, ANCO-1, BCL-3, BAF57. BRG1, CBP, CyclinD1, p300, GRIP1, NCoR, PGC-1, p72, PRMT1, PRMT2, 14-3-3 η, P/CAF	**SRC-1** AHR, ARNT, FOS, HIF1A, FOXA2, JUN, CIITA, NFKB1, SRF, STAT6, TEAD1, TITF1, YWHAQ
		SRC-2 AR, ERα, ERRβ, LRH1, GR, HNF4α, PPARγ, RORα. RARα, RXRα, SF1, TRβ, VDR			**SRC-2** ANCO-1, BAF57, BRCA1, CARM1, p300, GMEB-1, PRMT1, SRC-1, 14-3-3η	**SRC-2** AHR, ARNT, CCNT1, MAGEA11, TITF1, PPFIA1, SRCAP, tat
		SRC-3 AR, COUP-TFI, ERα, ERβ, ERR-β, LRH-1, GR, PPARα, PXR, RARα, RXRα, RXRβ, TRβ, VDR, Nur77			**SRC-3** ANCO-1, BAF57, BRCA1, CBP, CARM1, CyclinD1, p300, MMS19, P/ CAF, PRMT1, PIAS1, TBP, 14-3-3η	**SRC-3** BMP6, BMP7, E2F1, ERBB2, ETS1, ETS2, ETV1, GSK3B, IKBKB, MYC, NPAS2, EBAG9, YWHAQ, SUFU
Peroxisome proliferator receptor γ coactivator 1	PGC-1/ PPARGC1A	CAR, ERα, ERRγ, FXRα, GR, HNF4α, LXRα, PPARα, PPARγ, RXRα, TRβ	Critical roles in fat and carbohydrate metabolism and energy homeostasis. **Domain:** RNP-1	Metabolic, cardiovascular	FKHR, Sirt1, SRC-1, TRAP230, TRAP220, DRIP150	HCFC1, NRF1, USF2, SURB7, TRFP, G6PC, PCK1
Nuclear receptor corepressor	N-CoR/NCOR1	AR, ERα, GCNF, GR, PPARα, PPARγ, PPARδ, RARα, REVERBα, REVERBβ	Corepressor for the NR superfamily and other transcription factors; recruits histone deacetylases. **Domain:** SANT	Up-regulated in cancer	GPS2, HDAC3, HDAC4, TBLR1, PTα, Sin3A, SHARP, SMRT, SAP30, Sirt1, SF3A1, TBL1, TIF1β	BCL6, RUNX1T1, CBFA2T3, CCND2, CDKN2A, CHD1, CLK1, DACH1, ERBB2, ETS1, ETS2, HD, HSPA4, CD82, KIF11, MECP2, MYOD1, NFKB1, PDCD2, PHB, PML, CCL3, SKI, SMARCB1, SMARCC1, SMARCC2, CORO2A, ZBTB16, RDBP, FBAP4, TRIM33
SMRT/HDAC1-associated repressor protein	SHARP/MINT	PPARδ, RARα	Steroid-inducible corepressor; recruits histone deacetylases. **Domains:** RNP-1, SPOC	Up-regulated in cancer	CyclinE1, HDAC1, HDAC2. MTA2, NCoR, RBBP4, SMRT, SRA	DLX5, RBPSUH, MSX2, PAK1, SOX9, Antp, Ras85D, E2f, MBD3, Hivep1
Thyroid receptor-associated protein 220	TRAP220/ PPARBP; (DRIP205, MED1, CRSP200)	AR, CAR, ERα, ERβ, GR, HNF4α, PPARα, PPARγ, RORα, RARα, RXRα, TRα, TRβ, VDR, Nur77	NR coactivator and member of MEDIATOR transcriptional complex. **Domains:** Phosphopantetheine attachment site, GHMP kinase	Neurological; cancer; metabolic	BRCA1, PGC-1, PIMT, 14-3-3η	CDKN1A, CTSD, TFF1, CRSP7, YWHAQ, Gata1, Gata2, Gata3, Gata4, Gata6, MED9, IXL, MED28, MED25, MED10, MED19
Activating signal cointegrator-2	ASC-2/NCOA6; (NRC, PRIP, RAP250, TRBP, AIB3)	AR, CAR, CARβ, ERα, ERβ, GR, LXRβ, PPARα, PPARγ, RARα, RXRα, TRα, TRβ	Coactivator for NR superfamily and other transcription factors.	Mutated in cancers	Ku80, BCL-3, CBP, CoAA, CAPER, p300 NIF-1, PIMT, PARP-1, PRMT2	ASCL2, CD40, CEBPA, ATF2, CXADR, E2F1, FGR, FOS, XRCC6, GTF2A1, HSF1, JUN, NFKB1, NUMA1, RBBP5, SRC, SRF, TOP1, TUBA1, HBXIP, SRF, ASCC1, MLL3, TUBB
Silencing mediator of retinoid and thyroid receptors	SMRT/NCOR2	AR, ERα, GCNF, GR, PPARα, PPARγ, RARα, TRβ, Nur77	Corepressor for NR superfamily and others; recruits histone deacetylases. **Domain:** SANT	Cancer, metabolic, bone	HDAC1, HDAC2, HDAC3, HDAC4, NCoR, Sin3A, SKIP, SHARP, SAP30, Sirt1, TBL1	BIRC3, BCL6, RUNX1T1, CCND2, CDKN2A, CHUK, FOS, RBPSUH, IL8, MYBL2, MYOD1, NFKB1, NFKBIA, PML
cAMP response element-binding protein (CREB) binding protein	CBP/CREBBP	AR, ERα, GR, HNF4α	Coactivator for NR superfamily and other transcription factors; closely related to p300. **Domains:** Bromodomain, KIX, PHD-type zinc finger	Neurological	ASC-1, ASC-2, AIB1, BCL-3, BRG1, BRCA1, CtBP1, CITED1, CDC25B, Cyclin D1, Daxx, FKHR, JDP-2, MGMT, PIMT, p68, PELP1, PROX1, PIAS3, PT-α, RBBP4, RHA,	CDKN1A, CREB1, ATF2, CSK, E2F1, E2F3, FOS, GATA1, HOXB7, IRF3, JUN, SMAD1, MYB, MYOD1, NFATC2, SRF, and others
Receptor-interacting protein 140	RIP140/NRIP1	DAX1, ERα, GR, LXRα, PPARα, PPARγ, RARα, RXRα, RXRβ, SF-1, TR2	Bimodal coregulator, shown to function as a coactivator or corepressor; roles in metabolism.	Reproductive	CtBP1, CtBP2, HDAC1, HDAC3, 14-3-3η, P/CAF	AHR, FOXA1, JUN, POLR2A, MAP3K7, TRAF2, HDAC9, HDAC5, YWHAQ, LDOC1, TEX11, CEP70
Adenovirus E1A-associated 300kDa protein	p300/EP300	ERα, PPARα, PPARγ, PPARδ, RORα, RARβ, TRα, Nur77	Coactivator for NR superfamily and other transcription factors; closely related to CBP. **Domains:** Bromodomain, KIX, TAZ and PHD-type zinc fingers	Cancer, neurological	ASC-1, ASC-2, ADA3, AIB1, BCL-3, BRCA1, CtBP1, CITED1, CoAA, CARM1, Cyclin D1, p300, GPS2, GRIP1, JDP-2, MGMT, PIMT, PC2, PC4, p68, PELP1, PROX1, PIAS3, PT-α, SMAD3, SAF-A, STAT3, SRC-1, SYT,	Numerous
Coactivator-associated arginine methyltransferase1	CARM1/CARM1; (PRMT4)	NA	Arginine methylase; required for pluripotency of stem cells. **Domain:** Methyltransferase	Up-regulated in cancer	SRC-1, SRC-2, SRC-3	ELAV1, PABPN1, SRCAP
Steroid receptor RNA activator	SRA/SRA1	ERα, GR, MR, PR, AR	RNA transcript and an AF-1-specific transcriptional coactivator.	Up-regulated in cancer	PUS1, SHARP, SRC-1, SLIRP	NA
Transcription intermediary factor-1α	TIF1α/TRIM24; (CCCP)	AR, COUP-TFII, ERα, ERβ, GR, HNF4α, MR, PR, RARα, RXRα, VDR	Associates with chromatin. **Domains:** RBCC, bromodomain, PHD finger	Up-regulated in cancer	TIF1α, TIF1β	GTF2E1, HSPA1A, PML, TAF7, TAF11, ZNF10, CBX1, CBX3, CBX5, TRIM33
CAPER	CAPER/RBM39	ERα, ERβ, PR	Processes NR-regulated genes. **Domains:** RNP-1, CC1	NA	ASC-2	JUN, HSP70
Metastasis-associated 1	MTA1/MTA1	ERα	Corepressor; part of the NURD histone deacetylase complex. **Domains:** ELM2, SANT, BAH	Up-regulated in cancer	CDK7, HDAC1, HDAC2, MAT1, MTA2, MICoA, NRIF3, RBBP4, RBBP7, Sin3A, p53	ATR, CCNH, CHD4, FYN, GRB2, NCK1, MBD3L1
Coactivator activator	CoAA/RBM14	NA	Coactivator with roles in RNA splicing. **Domains** RNP-1	Up-regulated in cancer	Ku80, ASC-2, p300, PARP-1	TARBP2

See online version for legend and references.

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Nuclear receptors (NRs) are a superfamily of transcription factors regulated by the direct binding of endogenous, dietary, clinical, and xenobiotic ligands, as well as by cellular signaling pathways. To orchestrate programs of gene expression in specific tissues, NRs interact with a large, disparate class of molecules known as coregulators, which either potentiate (coactivators) or suppress (corepressors) expression of NR target genes. In previous SnapShots, *Nuclear Receptors I* and *Nuclear Receptors II*, we described the major functions of the NRs, including genes they target and diseases associated with their abnormal activities.

In this SnapShot, we present information about the coregulators of NRs. Coregulators integrate diverse signals in the cell, including those from NRs and other pathways, and then mediate a co-ordinated transcriptional response to these afferent signals. Reflecting this biology, coregulators are organized into multicomponent and multifunctional protein complexes. The terms "coactivator" and "corepressor" are context specific because the specific tissue, cell, and promoter influence the function of a given coregulator.

The table here describes the major functions of selected coregulators and diseases associated with their abnormal activity. The name of each coregulator is given as: Familiar Symbol/HGNC symbol (Other common names). In addition, the table lists NRs with which the coregulator has been shown to interact physically or functionally. Similar lists are provided for interactions with NR coregulators and other proteins.

Additional information about NR coregulators is available at the Nuclear Receptor Signaling Atlas (NURSA) Molecule Pages website (http://www.nursa.org) and in the references below. Specific literature on diseases associated with coregulators is at the Diseases and Phenotypes section of the NURSA Molecule Pages, whereas information about the coregulators' interactions with NRs and other transcription factors is at the Interactions section of the NURSA Molecule Pages. The ordering of coregulators in the table is based on visits to the NURSA Molecule Pages from May 2009–May 2010.

Abbreviations

bHLH, basic-helix-loop-helix; CAPER, coactivator of activating protein-1 and estrogen receptors; CC1, coiled-coil 1; CNS, central nervous system; DBD, DNA-binding domain; ERE, estrogen response element; GHMP, galacto-, homoserine, mevalonate, and phosphomevalonate kinase; HAT, histone acetyltransferase; NA, not available; NURD, nucleosome remodeling and histone deacetylase; PAS, Per, Arnt, Sim domain; PHD, Plant Homeo Domain; PP-binding, Phosphopantetheine attachment site; RNP-1, RNA-binding motif 1; SANT, switching-defective protein 3 (Swi3), adaptor 2 (Ada2), nuclear receptor corepressor (N-CoR), transcription factor (TF)IIIB'; TAZ, Transcription Adaptor putative Zinc finger.

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